REMARKS

Claims 1-110 are pending.

Claim Objections

Claims 33 and 76 were objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim, i.e., claim 31 or claims 74 and 33, respectively. Applicants respectfully traverse.

37 CFR 1.75(c) refers to claims in dependent form that "[refer] back to and further [limit] another claim or claims in the same application." Claim 33 is an independent claim, and does not "refer back to" claim 31, nor does claim 31 "refer back to" claim 33. Thus, the relationship between claims 33 and 31 is not encompassed by 37 CFR 1.75(c). Consequently, neither claim 33 nor claim 31 can be of "improper dependent form" with respect to the other.

Similarly, claim 76 is an independent claim that does not "refer back to" either claims 74 or 33, nor do claims 74 or 33 "refer back to" claim 76. Thus, the relationship between claim 76 and claims 74 and 33 is not encompassed by 37 CFR 1.75(c). Consequently, neither claim 76 nor claims 74 or 33 can be of "improper dependent form" with respect to the other.

Additionally, claim 31 depends from independent claim 22, which recites an "isolated antibody or fragment thereof obtained from an animal that has been immunized with a protein selected from the group consisting of..." whereas claim 33 recites an "isolated monoclonal antibody or fragment thereof that specifically binds to a protein selected from the group consisting of..." without reference to immunizing an animal. Therefore, claims 33 and 31 are of different scope. Therefore, this objection is improper and Applicants respectfully request withdrawal of this rejection.

Similarly, claim 74 depends from independent claim 69, which recites an "isolated antibody or fragment thereof obtained from an animal that has been immunized with a protein selected from the group consisting of..." whereas claim 76 recites an "isolated monoclonal antibody or fragment thereof that specifically binds to a protein selected from the group consisting of..." without reference to immunizing an animal. Therefore, claims 76 and 74 are of different scope. Additionally, claim 33 is directed towards a protein of SEQ ID NO:2, whereas claim 76 is directed towards a protein encoded by the cDNA contained in ATCC Deposit No. 97149. As discussed below, even though the SEQ ID NO:2 was obtained by sequencing the cDNA contained in ATCC Deposit No. 97149, the two are not necessarily identical in scope.

Therefore, this objection is improper and Applicants respectfully request withdrawal of this rejection.

The Examiner suggests that the syntax of claims 52, 69, 76 and 97 can be improved by amending part (b) to recite "in a host cell" rather than "from a host cell." Applicants respectfully disagree.

The polypeptide of the invention is a secreted protein. Therefore, it is expressed "from" a host cell, i.e., secreted into the extracellular space, rather than being expressed within the cell, i.e., in the intracellular space. The claims, by reciting the phrase "from a host cell," more accurately reflect this reality that the phrase "in a host cell," as suggested by the Examiner.

Claims 53, 55, 56, and 70, 72, 73 were objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, the Examiner alleges that these claims recite identical limitations of either claims 2-4, 8-9, or 23-25, 29-30, respectively, since the DNA encoding ATCC 97149 encodes the protein defined in claim 1. Applicants respectfully traverse.

As discussed previously, 37 CFR 1.75(c) refers to claims in dependent form that "[refer] back to and further [limit] another claim or claims in the same application." None of claims 53, 55, 56, or 70, 72, 73 "refer back to" any of claims 2-4, 8-9, or 23-25, 29-30, respectively. Thus, the relationship between these claims is not encompassed by 37 CFR 1.75(c) and the claims cannot be of "improper dependent form" with respect to the other.

Additionally, even though the nucleic acid sequence of SEQ ID NO:1, and hence, the deduced amino acid sequence of SEQ ID NO:2, were obtained by sequencing the cDNA contained in ATCC Deposit No. 97149, they are not necessarily identical. As indicated in the Brief Description of Figure 1, sequencing of the cDNA was performed using 373 Automated DNA Sequencer (Applied Biosystems, Inc.), which has an accuracy of ***greater than 97%***. Thus, the sequence of SEQ ID NO:1 (and thus SEQ ID NO:2) may differ from that of the cDNA contained in the Deposit (or the protein encoded by the deposit) due to sequencing errors. Additionally, the sequence of SEQ ID NO:1 or 2 may contain typographical errors, which could also result in the sequence being different from that of the cDNA contained in the Deposit or the protein encoded by the Deposit. As discussed in the M.P.E.P at §706.03(k), "court decisions have confirmed applicant's right to restate (i.e., by plural claiming) the invention in a reasonable number of ways. Indeed, ***a mere difference in scope*** has been held to be enough." [emphasis added]. Because a protein having the sequence of SEQ ID NO:2 may be different from the

protein encoded by the cDNA, Applicants submit that the claims have a sufficient "difference in scope." Applicants therefore request withdrawal of this objection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 18, 19, 49, 50, 65, 66, 88 and 89 were rejected under 35 U.S.C. §112, ¶2 as indefinite. Specifically, the Examiner asserts that it is unclear how a cell can produce a fragment of an antibody. Applicants respectfully traverse.

Applicants submit herewith a review article by Joosten et al. that was published on January 30, 2003. The review article describes the current status and views concerning the production of antibody fragments and antibody fusion proteins by yeasts and filamentous fugi. At page 4, the review article discusses production of recombinant antibody fragments by *E. coli*. At least two of the references mentioned in this discussion were published prior to the earliest priority date of the present application (See, for example, Better et al. (1988), and Skerra et al. (1988), abstracts of which are submitted herewith). Thus, as of the filing date of the application, one of skill in the art was able to generate a cell capable of expressing an antibody fragment. Applicants therefore request withdrawal of this rejection.

Double Patenting

Claims 1-5, 8-10, 22-26, 29-37, 40-42, 52-66, 69-89 and 97-110 were provisionally rejected over claim 14 of Application No. 10/060,523, claim 20 of Application No. 10/120,398, claim 21 of Application No. 10/120,377 and claim 21 of Application No. 10/120,414.

Applicants will consider filing a Terminal Disclaimer in the present application over the any of claims 14, 20, 21 or 21, as currently pending in U.S. Application No. 10/060,523, 10/120,398; 10/120,377 and 10/120,414, respectively, if any of claims 14, 20, 21 or 21 issue prior to allowance the currently pending claims in the instant application. Alternately, Applicants will consider canceling some or all of the cited claims in the copending applications.

Rejections under 35 U.S.C. §102 and 103

Claims 1-5, 10, 22-26, 31-37, 42, 52-54, 57-66, 69-71, 74-78, 81-89, and 97-100 were rejected under either or both of 35 U.S.C. §102(b) as anticipated by Houck et al. or 35 U.S.C. §103(a) as unpatentable over Houck et al. in view of Colwell et al. Applicants respectfully traverse.

As acknowledged by the Examiner, Houck et al. disclose a protein (VEGF) the use of a monoclonal antibody to immunoprecipitate the VEGF protein.

As discussed at Section III(C) (page 5) of the Roschke Declaration (submitted with Applicants' previous response), the term "specifically" is used by one of skill in the art to refer to an antibody that binds a polypeptide in one species (*e.g.*, human) and also, perhaps, an orthologous polypeptide in another species (*e.g.*, mouse). That is, the use of the term "specifically" includes an antibody that binds both human Protein-X and murine Protein-X. Such cross-species binding was (and is) merely understood to indicate that the antigenic determinant to which the Protein-X antibody binds is conserved in both the human and mouse Protein-X orthologs.

In contrast, an antibody that binds equally well to human Protein-X and human Protein-Y (*i.e.*, paralogous polypeptides) would not be an antibody that an immunologist would have considered as one that "specifically" bound Protein-X.

As discussed in Footnote 1 of the Roschke Declaration, orthologous genes (or, genes which are orthologues) are derived from a common ancestor through vertical evolutionary descent. Thus, genes (and proteins encoded by them) are considered to be orthologues when they represent the *same* gene (or protein) found in *different* species. For example, feline FGF-1 (fibroblast growth factor-1), murine FGF-1, and human FGF-1 are orthologues (orthologous proteins). In contrast, paralogous genes (or, genes which are paralogues) are genes found within the same genome that are thought to have evolved by gene duplication. For example, human FGF-1, human FGF-2, and human FGF-3 are gene paralogues; and, the proteins encoded by these genes are also paralogues (or paralogous proteins).

Thus, according to the art-accepted definition of a paralogue, the VEGF protein disclosed by Houck et al. is a paralogue of VEGF-C claimed in the instant application. Therefore, an antibody that binds both the VEGF protein and the VEGF-C protein would not be considered by a skilled artisan to be an antibody that "specifically binds" the claimed VEGF-C

protein. Consequently, use of the term "specifically binds" in the claims distinguishes the claimed invention over the disclosure of Houck et al.

Nothing in the disclosure of Colwell et al. remedies the deficiencies of Houck et al. Therefore, Applicants respectfully request the withdrawal of this rejection.

CONCLUSION

Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

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Respectfully submitted,

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